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EXAMINER	
CUNNINGHAM T	
ART UNIT	**PAPER NUMBER**
1813	8

18N1/0328

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DATE MAILED: 03/28/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 1/17/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-43 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-43 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

15. Claims 1-43 are active.

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as the invention.

17. Claims 1, 4 and 31 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what the metes and bounds of the term "nonimmunogenic" are. The administration of the claimed products and compositions appears to result in a down regulation of the immune system. Does "non-immunogenic" refer to the inability of a particular composition to induce an antibody or cellular immune response? Does this mean that the claimed compositions are also incapable of inducing suppressor T cells, or other suppressive immune phenomena such as high or low zone tolerance, which would be expected to down-regulate antigen-specific immune responses?

18. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using

> it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately describe or enable the claimed invention.

A. It appears that the peptides used in the claimed compositions and methods are "immunogenic" as they induce immune responses in human patients, see e.g. page 23, line 26 of the specification. Thus, the claim limitation to use of "nonimmunogenic" peptides is not adequately supported. Perhaps an alternative term such as "tolerogenic" would be better supported.

B. The test data from the human Phase II study disclosed on page 24, line 2 of the specification cannot be adequately evaluated because the results are presented as a summary, e.g. the total allergy score of 80% of the patients improved. How is the total allergy score calculated? Were the study results statistically significant vis-a-vis control group total allergy scores?

C. The specification does not adequately describe the amino acid sequences of Amb a I peptide antigens, which portions of the Amb a I antigen would be nonimmunogenic, nor provide adequate

guidance as to which Amb a I peptides would reduce allergic responses to ragweed allergy in humans. Further, it would be unpredictable which dosages and routes of administration could be used with particular peptides. For instance, it would be unpredictable whether a particular peptide would induce tolerance by inducing suppressor T cells or affecting IgE responses when given orally or sublingually as peptidases and anatomic barriers in these sites would affect the biological half life and uptake of the peptide. Applicant may wish to consider incorporation of the essential portions of WO93/21321 which may describe particular Amb a I peptides into the instant specification.

19. Claims 1-43 are rejected under 35 U.S.C. 112, first paragraph for the reasons set forth in the objection to the specification.

20. Assuming the validity of the Phase II data on Peptide X and Peptide Y, claims 1-43 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the particular antigens described in the specification, e.g. Peptide X and Peptide Y derived from the feline antigen, Fel d I. One with skill in the art would not have been enabled to make and use compositions or methods to treat allergic or autoimmune diseases without guidance as to which antigens are associated

with particular autoimmune or allergic diseases. For instance, the specification does not disclose the autoantigens associated with the autoimmune diseases multiple sclerosis or diabetes. Secondly, in the absence of description by the disclosure, it would be unpredictable which portions of particular antigens would be nonimmunogenic, or what the amino acid sequences of such nonimmunogenic portions would be. Administration of immunogenic portions of an autoantigen or allergen would be expected to increase, rather than decrease the severity of allergic or autoimmune diseases. Therefore, one with skill in the art would not be enabled to make and use compositions to treat such diseases. See M.P.E.P. §§ 706.03(n) and 706.03(z).

21. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

23. Claims 1-43 are rejected under 35 U.S.C. § 103 as being unpatentable over Sehon et al., J. Allergy Clin. Immunol. 64:242-250 (1979), Michael et al, U.S. patent 4,338,297 (issued 1982) or Litwin et al., Clin. Exp. Allergy 21:457-465 (1991) or Kuo et al., U.S. patent 5,328,991 (filed 1991). The claims are broadly drawn to therapeutic compositions comprising various determinants of allergens or autoantigens and to methods of treating sensitivity to allergens or autoantigens using such compositions.

Sehon et al. teach a variety of methods of making tolerogens from allergens and using such tolerogens to induce tolerance to particular allergens. Michael et al. teach how to make and use proteolytic fragments of pollen allergens to desensitize subjects to allergy. Litwin et al. teach how to make and use immunosuppressive peptide fragments of allergens to treat allergy. Kuo et al., see abstract and claims, teach modified Fel d I antigen and its use for inducing tolerance in cat allergic subjects.

It would have been prima facie obvious to one of ordinary skill in the art to use the methods of the cited references to make modified, nonimmunogenic allergen preparations for use in methods of desensitizing or inducing tolerance to particular allergens or autoantigens. Routine optimization of the dosage and mode of administration of the instant compositions fall within the ordinary skill of the art as evidenced by the cited references. Thus, claims 1-43 are prima facie obvious over the cited prior art.

24. Papers related to this application may be submitted to Group 1800 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Thomas Cunningham, Art Unit 1813 and should be marked either "OFFICIAL" for entry into the prosecution history or "DRAFT" for consideration by the Examiner without entry. The Art Unit 1813 FAX telephone number is (703) 305-7939. FAX machines will be avaiLable to receive transmissions 24 hours a day.

25. In compliance with 1096 OG 30 the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or federal

holiday with the District of Columbia, in which case the official date of receipt will be the next business day.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas M. Cunningham, Ph.D, J.D. whose telephone number is (703) 308-3968. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Thomas Cunningham

THOMAS M. CUNNINGHAM
PATENT EXAMINER
GROUP 1800